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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,600	02/20/2004	Jae C. Schwartz	12671-029001	1552

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EXAMINER	
JOHNSTON, PHILLIP A	

ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,600	SCHWARTZ, JAE C.	
	Examiner	Art Unit	
	Phillip A. Johnston	2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☒ Claim(s) *4,5,24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. This Office Action is submitted in response to amendment dated 9-22-2005, wherein claims 1,2,4,6,19,20,21,24,39 and 40 are amended. Claims 1-40 are pending.

Claims objection

2. Claims 4,5,24, and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

3. Claims 4,5,24, and 25 are allowed.

4. Claims 4,5,24, and 25 are allowed because prior art fails to show that, calculating a gain comprises: calculating a ratio of intensity values for at least two of the ions having different m/z values; and calculating a gain based at least in part on the ratio of intensity values.

Claims Rejection - 35 U.S. C. 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2,8, and 15-22 stand rejected under 35 U.S.C. 102 (b) as being clearly anticipated by Buckley, U.S. Patent No. 5, 463,219.

Buckley (219) discloses;

(a) A conventional inductively coupled plasma mass spectrometer (ICP-MS) that includes a sample source 12, which supplies a sample contained in a carrier gas (e.g. argon) through a tube 14 into a quartz tube 16 which contains a plasma 18, ion optics 50, a mass analyzer 64 which is typically a quadrupole mass spectrometer but may be a different form of mass analyzer, e.g. an ion trap. Ions passing through the mass spectrometer 64 are detected by electron multiplier detector 66, the output of which is processed by a processing circuit 68, as recited in claims 1, and15-18; See Column 5, line 20-67; Column 6, line 1-22; and Figure 1 below;

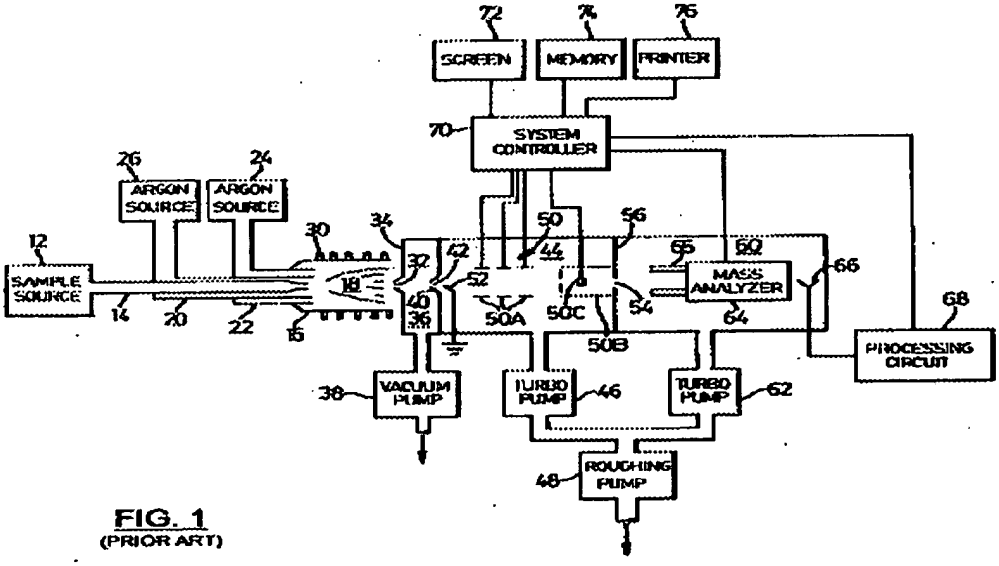

FIG. 1
(PRIOR ART)

(b) FIGS. 14A to 14E show calibration curves 302 to 310 for the substances cadmium, cerium, copper, magnesium, and rhodium respectively. In each case

analog intensity is plotted on the vertical axis and pulse counts are plotted on the horizontal axis. The curves 302 to 310 are each measured at a number of points in the overlap region 134 again determined by ramping the lens 50, and a straight line is fitted through the resultant points. The slope of the line is determined and the gain is computed from the slope. The quality of the line is visually displayed as well as indicated by the correlation coefficient. The resultant gain values are then plotted against mass as shown in FIG. 15 to yield a gain curve 312. From curve 312 the instrument can determine the relationship between gains and masses at positions between the measured points (e.g. by interpolation), as recited in claims 1,2,8, and 19-22. See Column 16, line 45-62; Figure's 14A-14E; and Figure 15 below.

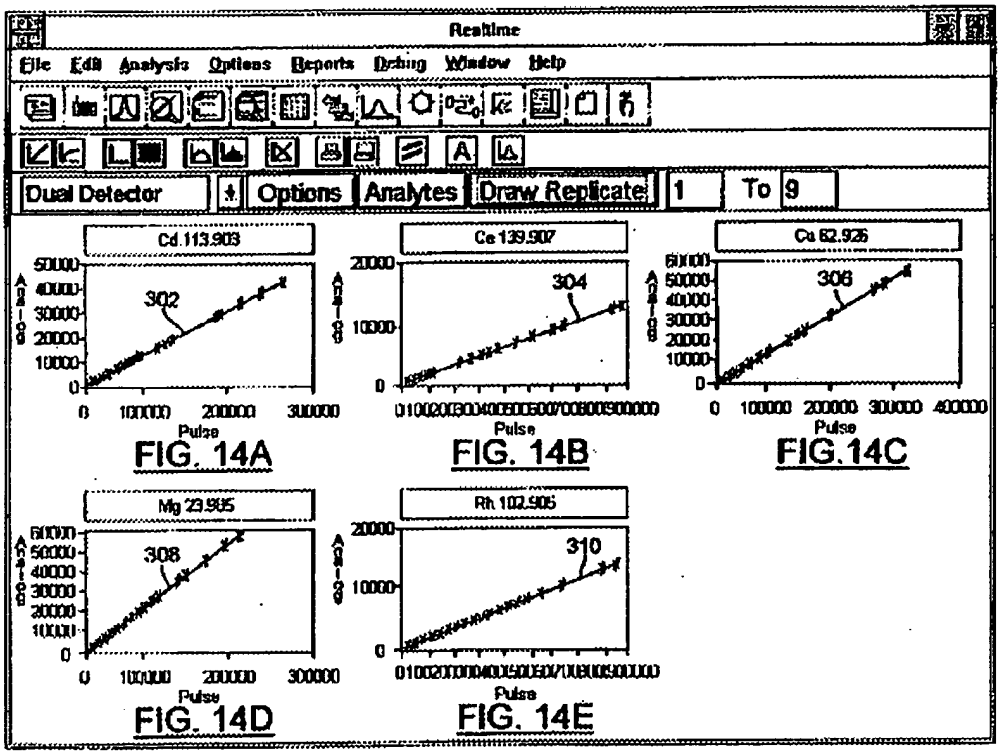

FIG. 14A FIG. 14B FIG. 14C

FIG. 14D FIG. 14E

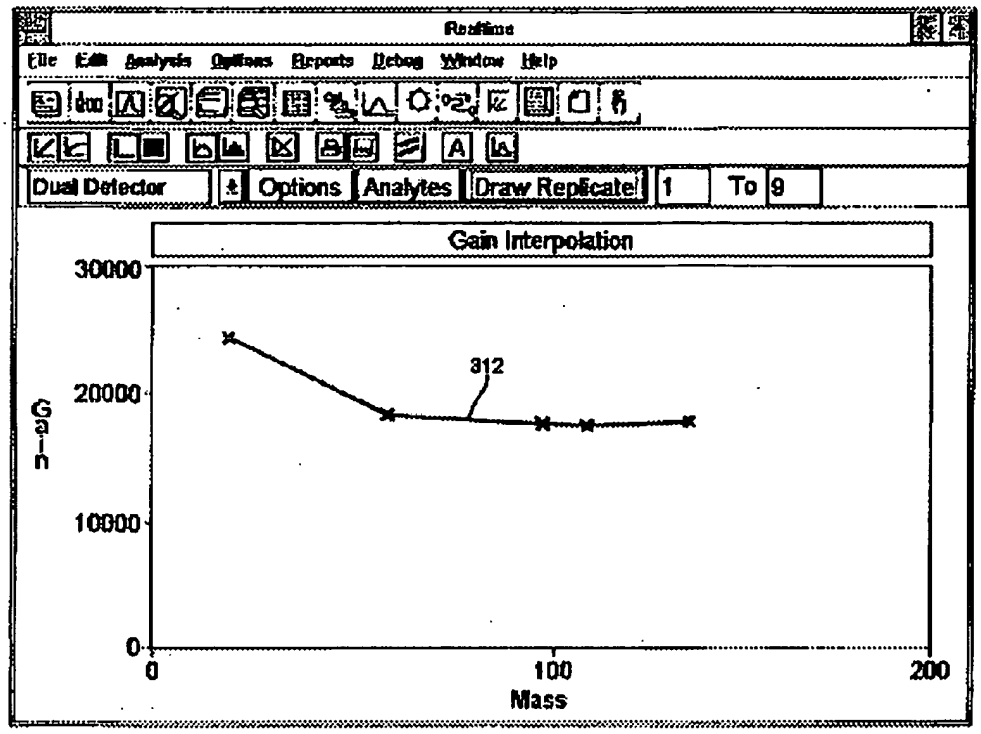

FIG. 15

Claims Rejection – 35 U.S.C. 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 3-7,9-13, 23-33, and 35-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,463,219 to Buckley, in view of Shimomura, U.S. Patent No. 6,265,714.

Buckley (219) describes source 12, as used in U.S. Pat. No. 4,746,794 (French et al.), which is an unstable atmospheric ion source, as recited in claims 9-13, 31-33, and 36. See Column 5, line 23-27; and line 58-60 in Buckley (21); as well as, Column 3, line 61-68; and Column 4, line 1-17 in French (794) .

Buckley (219) as applied above discloses nearly all the limitations of claims of claims 3-7, 23-28, 39 and 40, but fails to teach calculating gain or number of ions based upon formulas, as recited in claims 3-7, 23-28, 39 and 40.

However, Shimomura (714) discloses that after the specified number of sampling has been completed, the control unit 20 reads out the stored intensity data and obtains therefrom the average intensity and the standard deviation, as well as their ratio (hereinafter referred to as the "deviation-to-average ratio"). These numerical data are also stored in the memory device 21 so as to serve as the data for determining the detector degradation, as recited in claims 3-7, 23-28, 39 and 40. See Column 4, line 34-47.

Therefore it would have been obvious to one of ordinary skill in the art that the mass spectrometer apparatus and method of Buckley (219) can be modified to use the standard deviation method of Shimomura (714), to provide means for monitoring the level of degradation of a detector, thereby providing means for monitoring the stability of a mass spectrometer.

It is implied herein that calculating gain and number of ions from the slope of the intensity vs. ion pulse count curve as described above in Buckley (219) is equivalent to the use of formula's, as recited in claims 3,5,7,23,25, and 27.

9. Claims 14 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buckley (219) and Shimomura (714), and in further view of Kammei, U.S. Patent No. 6,674,068.

The combination of Buckley (219) and Shimomura (714) fails to disclose the use of a pulsed analyzer, as recited in claims 14 and 34. However, Kammei (068) discloses the use of an inductively coupled plasma source in a pulsed TOF mass spectrometer to measure ion intensity and control detector gain, as recited in claims 14 and 34. See Column 5, line 41-67; Column 1, line 1-11; and Column 9, line 1-11.

Therefore it would have been obvious to one of ordinary skill in the art that the mass spectrometer apparatus and method of Buckley (219) and Shimomura (714) can be modified to use the standard deviation method of Kammei (068), to provide means for storing an output signal from an ion detector indicative of the ion pulses together with information about the gain during detection such that the stored signal is correlated to the stored information about the gain.

Examiners Response to Arguments

10. Applicant's arguments filed 9-22-2005 have been fully considered but they are not persuasive.

Argument 1

The applicant states that "Buckley teaches a calibration procedure in which, during calibration for one substance, which is effectively one mass-to-charge ratio, the analog intensity is plotted on the vertical axis, and the number of ions hitting the detector on the horizontal axis. From this plot, the gain for this one substance can be calculated using the pulse count and the analog intensity signal. A plot is made of the analog intensity measured against pulse counts for different substances, that is for different mass-to-charge ratios. From each plot, a different gain can be determined, each gain being determined from the slope of a particular m/z ratio. Buckley then goes on to describe (starting at column 16, line 56) that the resultant gain values are then plotted against mass. Buckley does not teach or suggest how a direct relationship between gain and intensity of a plurality of mass-td-charge ratios can be used to calculate a gain of a detector. Instead, Buckley teaches that several steps are required to calculate the gain. The first gain calculation is based on ion intensity measurements of one mass-to-charge ratio. The gain results are then used to create a gain curve, and from this gain curve, subsequent gains can be determined for any mass, but not directly from any ion intensity measurements from a plurality of mass-to-charge ratios, but only indirectly therefrom. In other words, the direct calculation limitation set forth in amended claim 1 distinguishes the claimed subject matter from techniques, such as that taught in

Buckley, where at least one intervening step must be executed between the acquisition of intensity measurements and the calculation of gain."

The applicant is respectfully directed to applicants published specification paragraphs [0050], [0051],[0060], and [0061], which state;

[0050] Once, N, the number of ions measured is known, the detector gain G can then simply be calculated using the input total charge of these N ions and the measured output charge after electron multiplication. The output charge can readily be calculated given a measured or digitized intensity, since the transfer function, k, of the detector electronics associated with the output of the multiplier is fixed and known from the circuitry. Therefore

$$G = \frac{\frac{\bar{I}_1}{k}}{N}.$$

[0051] As stated previously, the critical component of the process of determining the gain is to accurately determine N, the number of ions measured.

[0059] For this situation the affects of S are eliminated. Consequently, by measuring the average ion intensity ratio, $\overline{I_{mR}}$ and its associated standard deviation σ_{mR}, then the relationship,

$$\sigma_R^2 = \left\{ \frac{\sigma_{N_a}^2}{N_a^2} + \frac{\sigma_{N_b}^2}{N_b^2} \right\} * (\overline{I_{mR}})^2$$

[0060], which is based on substitutions using $I_{ak}*G*N_a$ and $I_b = k*G*N_a$, along with their associated standard deviations $\Sigma_a=k*G\sigma_{Na}$ and $\sigma_b=k*G\sigma_{Nb}$ can be rearranged to yield that the average number of ions in any given first peak can be determined by

$$\overline{N_c} = \frac{(\overline{I_{mR}})^2(1+\overline{I_{mR}})}{\sigma^2_{mR}},$$

[0061] Given that the number of ions N is now determined, calculation of the detector gain G is straight forward using the transfer function of the detector electronics, k, the measured average intensity of the single peak, (I_{ma}) and by using the relationship

$$G = \frac{\frac{\overline{I_{mc}}}{k}}{\overline{N_c}},$$

The examiner has interpreted from the applicants references above that performing the step of measuring the average ion intensity ratio $\overline{I_{mR}}$ prior to determining the number of ions N, is an intervening step that is executed by the applicant between the acquisition of ion intensity measurements and the calculation of gain, and therefore detector gain is not calculated directly from ion intensity measurements, as recited in the amended claims.

The applicant is respectfully directed to the Abstract in Buckley (219), which states; A mass analyzer system uses a simultaneous mode electron multiplier detector which outputs both a pulse count and an analog signal. Depending on the ion flux intensity, the signals define a pulse count only region in which the pulse count only signal is valid, an overlap region in which both the pulse count and analog signals are valid, an analog signal only region in which only the analog signal is valid, and a neither analog nor pulse region in which neither signal is valid. The system produces a separate flag for each region. When a mass spectrum is scanned, for each dwell the

pulse count and analog data are recorded together with their associated flag and are placed in memory. The signals, with the flags, can then be used to produce a mass spectrum using the pulse count only signal, the analog only signal, or both. In addition numeric displays can be produced for each peak or a variety of peaks, using the pulse count only signal, the analog signal, or both, together with a display of the flag or flags which have been set at the peak being displayed.

Also Figure 5 below; and Column 7, line 22-25, which states;

In FIG. 5 the effective ion count signal (counts per second) is plotted on the vertical axis. The horizontal axis shows the analog signal, converted to a frequency as will be explained. FIG. 5 is exemplary since the slope and intercept of the curve will vary with gain, as will be described.

In FIG. 5 four regions are shown. The first region 132 is a pulse only region, in which only the pulse count signal is used (although analog data is also continuously available). In this region the analog signal is either too low to be useful or is less useful than the pulse signal. As shown in the drawing, the pulse only region is marked by a flag (0, 0), as will be explained. The boundary between the region 132 and the next region 134 is empirically set, and in region 132 only pulse count data is arbitrarily considered to be "valid" (although the analog data can still be used, as will be described).

The second region 134 is an overlap region. Here, both the pulse and the analog signals are considered to be valid. Hence this region can be used to calibrate the analog signal to the pulse signal; therefore, this region is also referred to as a

calibration region. As will be explained, the overlap or calibration region 134 is marked by a flag (0, 1).

In the third region 136, the analog signal is sufficiently high that the voltage on pulse protect dynode 102 has been switched to 0 volts (for the ETP detector), shutting down the second stage 84 of the multiplier 66. This region is therefore an analog signal only region and is marked by flag (1, 1). Any pulse count data received in this region is clearly invalid.

In the fourth region 138, the analog signal has become so high that a detector protection voltage is applied (as will be explained) to de-focus ion lens 50, reducing the incoming ion flux by a large factor (e.g. 104), to protect the detector 66. This region, referred to as a "neither pulse nor analog" region, is marked by a flag (1, 0). Any pulse or analog data received in this region is also clearly invalid.

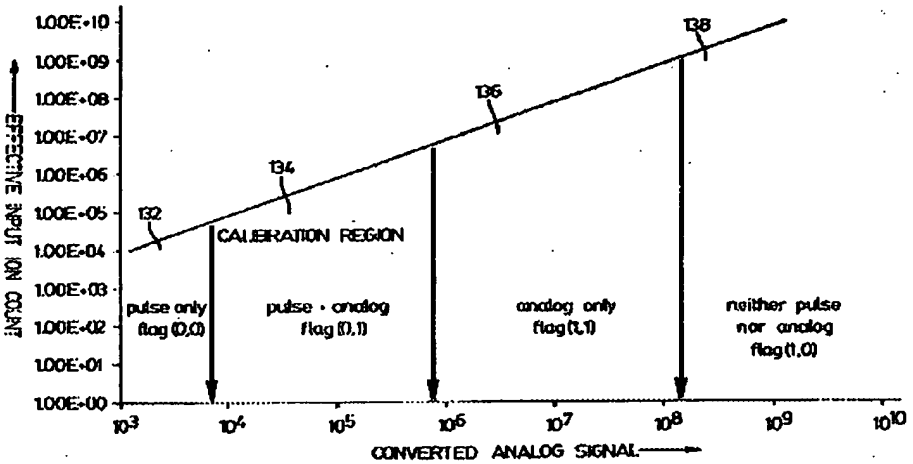

FIG. 5

As well as, Column 13, line 48-67; and Column 14, line 1-40, which states; If the input current produced by the ions incident on the detector is I_{IN}, and if the output or analog current is I_A, then there is a fixed relationship between the two: $I_A = f(G, I_{IN})$,

where G is the gain. The gain is determined by -V applied, which determines the total number of electrons ejected per incident ion. In cases where I_A exceeds several microamperes, a typical electron multiplier tends to saturate and f(G, I_{IN}) has an exponential dependence. Therefore the gain G is preferably selected such that saturation does not occur. Under these conditions there is a simple linear relationship:

$I_A = I_{IN}\ G$ (1)

In addition, I_{IN} =nc, where n is the number of ions/second and c is the Faraday constant (1,602 $X10^{-19}$ coulombs/charge).

Therefore I_A =ncG. (2)

It can therefore be seen that the maximum desired input count rate n, determines the desired gain for a fixed output current, I_A. Prototype experiments were performed to demonstrate that a typical detector maintains a linear response up to at least I_A = 2 microamperes. Therefore, for example, if I_A = 2 microamperes and if the desired maximum count rate $n=10^9$ cps, then G=1.25 $X10^4$. Similarly, if $n=10^{10}$ cps, then for I_A =2 micro amperes, then G=1.25 $X10^3$, etc. Thus the user can choose a target gain to select accordingly a maximum effective input count rate, and therefore the dynamic range of the detector system.

The examiner has interpreted from the Buckley (219) references above that gain G is calculated directly from the detector input count rate n, as recited in amended claims 1,19-21,39, and 40.

Conclusion

11. The Amendment filed on 9-22-2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the Buckley (219) references.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications should be directed to Phillip Johnston whose telephone number is (571) 272-2475. The examiner can normally be reached on Monday-Friday from 6:30 am to 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiners supervisor John Lee can be reached at (571) 272-2477. The fax phone number for the organization where the application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PJ
February 3, 2006

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SUPERVISORY PATENT EXAMINER
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